

*(use as many sheets as necessary)*

Sheet

1

**of**

3

**Application Number**

10/533,028

**Filing Date**

**April 26, 2005**

**First Named Inventor**

**George D. Hartman**

## Group Art Unit

~~To Be Assigned~~

**Examiner Name**

### To Be Assigned

Attorney Docket Number

20942P

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**Examiner  
Signature**

Date Considered

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		Application Number	10/533,028		
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		First Named Inventor	George D. Hartman		
		Group Art Unit	<del>To Be Assigned</del> 1624		
		Examiner Name	To Be Assigned		
Sheet	2	of	3	Attorney Docket Number	20942P

NON PATENT LITERATURE DOCUMENTS		
Examiner Initials*	Cite No.	Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.
DR	3	Amirkhosravi, A., et al., "Blockade of GpIIb/IIIa inhibits the release of vascular endothelial growth factor (VEGF) from tumor cell-activated platelets and experimental metastasis", Platelets, 10, pp. 285-292 (1999)
	4	Brockelsby, J., et al., "VEGF Via VEGF Receptor-1 (Flt-1) Mimics preeclamptic Plasma in Inhibiting Uterine Blood Vessel Relaxation in Pregnancy: Implications in the Pathogenesis of Preeclampsia", Laboratory Investigation, 79, pp. 1101-1111 (1999)
	5	Carlson, B.A., et al., "Flavopiridol Induces G1 Arrest with Inhibition of Cyclin-dependent Kinase (CDK) 2 and CDK2 in Human Breast Carcinoma Cells", Cancer Research, 56, pp. 2973-2978 (1996)
	6	Deckers, M.M.L., et al., "Expression of Vascular Endothelial Growth Factors and Their Receptors during Osteoblast Differentiation", Endocrinology, 141, pp. 1667-1674 (2000)
	7	Detmar, M., "The role of VEGF and thrombospondins in skin angiogenesis", Journal of Dermatological Science, 24, Suppl. (1), pp. S78-S84 (2000)
	8	Dickinson, A.J., et al., "Quantification of angiogenesis as an independent predictor of prognosis in invasive bladder carcinomas", British Journal of Urology, 74, pp. 762-766 (1994)
	9	Ellis, L.M., et al., "Down-regulation of vascular endothelial growth factor in human colon carcinoma cell lines by antisense transfection decreases endothelial cell proliferation", Surgery, 120, (5), pp. 871-878 (1996)
	10	Gasparini, G. and Harris, A.L., "Clinical Importance of the Determination of Tumor Angiogenesis in Breast Carcinoma: Much More Than a New Prognostic Tool", Journal of Clinical Oncology, 13, pp. 765-782 (1995)
	11	Gerber, et al., "VEGF couples hypertrophic cartilage remodeling, ossification and angiogenesis during endochondral bone formation", Nature Medicine, Vol. 5, (6), pp. 623-628 (1999)
	12	Giatromanolaki, A., et al., "The angiogenic pathway 'vascular endothelial growth factor/flk-1(KDR)-receptor' in rheumatoid arthritis and osteoarthritis", Journal of Pathology, 194, pp. 101-108 (2001)
	13	Glab, N., et al., "Olomoucine, an inhibitor of the cdc2/cdk2 kinases activity, blocks plant cells at the G1 to S and G2 to M cell cycle transitions", FEBS Letters, 353, pp. 207-211 (1994)
	14	Greenberg, D.A., "Angiogenesis and Stroke", Drug News Perspect, 11, pp. 265-270 (1998)
	15	Gunningham, S.P., et al., "Vascular Endothelial Growth Factor-B and Vascular Endothelial Growth Factor-C Expression in Renal Cell Carcinomas: Regulation by the von Hippel-Lindau Gene and Hypoxia", Cancer Research, 61, pp. 3206-3211 (2001)
	16	Hasegawa, T., et al., "Intracortical osteoblastic osteosarcoma with oncogenic rickets", Skeletal Radiology, 28, pp. 41-45 (1999)
↓	17	Jain, R.K., "Normalizing tumor vasculature with anti-angiogenic therapy: A new paradigm for combination therapy", Nature Medicine, Vol. 7, (9), pp. 987-989 (2001)

Examiner Signature	<i>Deepak K. B.</i>	Date Considered	4/8/06
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Examiner Initials*	Cite No.	Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.
OR	18	Kelland, L.R., "Flavopiridol, the first cyclin-dependent kinase inhibitor to enter the clinic: current status", Expert Opinion on Investigational Drugs, 9, pp. 2903-2911 (2000)
	19	Kitagawa, M., et al., "Butyrolactone I, a selective inhibitor of cdk2 and cdc2 kinase", Oncogene, 8, pp. 2425-2432 (1993)
	20	Levis, M., et al., "A FLT3 tyrosine kinase inhibitor is selectively cytotoxic to acute myeloid leukemia blasts harboring FLT3 internal tandem duplication mutations", Blood, Vol. 98 (3), pp. 885-887 (2001)
	21	Losiewicz, M.D., et al., "Potent Inhibition of CDC2 Kinase Activity By The Flavonoid L86-8275", Biochemical and Biophysical Research Communications, 201, pp. 589-595 (1994)
	22	Nakagawa, M., et al., "Vascular endothelial growth factor (VEGF) directly enhances osteoclastic bone resorption and survival of mature osteoclasts", FEBS Letters, 473, pp. 161-164 (2000)
	23	Paul, R., et al., "Src deficiency or blockade of Src activity in mice provides cerebral protection following stroke", Nature Medicine, 7, pp. 222-227 (2001)
	24	Rak, J., et al., "Mutant ras Oncogenes Upregulate VEGF/VPF Expression: Implications for Induction and Inhibition of Tumor Angiogenesis", Cancer Research, 55, pp. 4575-4580 (1995)
	25	Senderowicz, A.M., "Flavopiridol: the first cyclin-dependent kinase inhibitor in human clinical trials", Investigational New Drugs, 17, pp. 313-320 (1999)
	26	Smith, Stephen K., "Regulation of angiogenesis in the endometrium", Trends in Endocrinology & Metabolism, Vol. 12, (4), pp. 147-151 (2001)
	27	Toi, M., et al., " Association of Vascular Endothelial Growth Factor Expression with Tumor Angiogenesis and with Early Relapse in Primary Breast Cancer", Japan. J. Cancer Res., 85, pp. 1045-1049 (1994)
	28	van der Flier et al., "Vascular Endothelial Growth Factor in Bacterial Meningitis: Detection in Cerebrospinal Fluid and Localization in Postmortem Brain", J. Infectious Diseases, 183, pp. 149-153 (2001)
✓	29	Williams, J.K., et al., "Tumor Angiogenesis as a Prognostic Factor in Oral Cavity Tumors", American Journal of Surgery, 168, pp. 373-380 (1994)

Examiner Signature	Deepak K. Singh	Date Considered	4/8/06
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